REMARKS

As a preliminary matter, Applicants acknowledge and appreciate the allowability of Claims 10 and 18. Applicants also acknowledge that a new examiner has been appointed and would like to call attention to the fact that in the Office Action dated August 18, 2005, it was stated that Claims 14-18, 20-23, 41, 47, 69 and 95-101 are drawn to allowable subject matter, noting that Claim 96 had been objected to.

In the outstanding non-final Office Action dated April 5, 2006, the Examiner has rejected claims previously indicated to be allowable.

Reconsideration of the above referenced application is respectfully requested. Upon entry of the foregoing amendment, Claims 1, 4-8, 10-11, 14-18, 20-23, 41, 47, 69, and 95-101 are currently pending. Claims 2-3, 9, 12-13, 19, 24-40, 42-46, 48-68, 70-94, 96 and 102-103 have been canceled without prejudice or disclaimer. Claims 5, 14, 18, 69, 95, and 97 have been amended. Basis for the amendments may be found throughout the specification and in the claims as originally filed. No new matter has been introduced and entry of the amendment is requested.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1, 5, 14, 69, 97, 100, and 101 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5, 100, and 101 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite based on the statement on pages 3 and 4 of the Office Action that claims 100 and 101 are outside of the scope of claim 1.

Applicants respectfully disagree. Claims 100 and 101 make reference to SEQ ID NO:8 which comprises the partial tripartite leader sequence found in pCLF. The plasmid map for pCLF shown in FIG. 4, indicates that pCLF comprises an Ad2 leader sequence and an Ad5 fiber sequence. The corresponding cDNA sequence of the partial tripartite leader sequence found in pCLF is listed in SEQ ID NO: 8 bordered by BamHI/BglII 5' and 3' sites at respective nucleotide

positions 907-912 to 1228-1233. (See paragraph 278 of the published version of the instant application; US Patent Pub. No. 20030157688.

Claim 5 stands rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite based on the statement on page 2 of the Office Action. Claim 5 is no longer dependent on Claim 1, obviating the basis for rejection.

Claim 14 stands rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite based on the statement on pages 3 and 4 of the Office Action that the relationship between claim 14 i) and ii) is not clearly defined. Claim 14 has been amended to clarify that the TPL sequences in 14 i) and ii) are the same.

Claim 69 stands rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite because it is not clear what "said stably integrated nucleic aid molecule" is. Claim 69 has been amended to clarify what a "said stably integrated nucleic acid molecule" is.

Claims 97 stands rejected under 35 U.S.C. §112, second paragraph as allegedly incomplete for omitting essential elements, such omission amounting to a gap between the elements. Claims 95 and 97 have been amended to add the step of introducing into said packaging cell line a recombinant adenovirus vector genome.

Applicants respectfully submit that the grounds for the various rejections under 35 U.S.C. § 112, second paragraph have been obviated by the amendments described above. Withdrawal of the rejections is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1, 4-8, 11, 14-23, 41, 47, 69, 95, 97, 98, and 99 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth on pages 5 - 8 of the Office Action.

On pages 5 and 6, the Office Action further details the rejection of Claims 1, 4-8 and 11 and states that Applicants has disclosed an isolated nucleic acid molecule which contains an Ad5 TPL, however, Applicant has not disclosed a TPL from different Ad species.

Applicants disagree, and respectfully submit that the specification meets Applicants' burden under 35 U.S.C. 112, first paragraph, and provides a sufficient number of species to support the presently pending claims.

The guidelines for determining compliance with 35 U.S.C. 112 note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants note that recitation in a claim of a generic element, for example a TPL nucleotide sequence, does not require that the specification list each and every TPL sequence that might be used with the invention. Indeed, as set forth in the MPEP: a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies , Inc .*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Paragraph [0156] of the published version of the instant specification specifically states that "preferably the TPL exons are from Ad2, Ad3, Ad5, Ad7 and the like, however, they may come from any Ad serotype, as described herein."

Hence, one of ordinary skill in the art would be informed by the teachings of the subject specification, as to how to make an isolated nucleic acid molecule which contains an Ad TPL

from an Ad species other than Ad and which comprises TPL exons from different adenoviruses, according to Claims 1, 4-8 and 11. In view of the above amendments and remarks, withdrawal of the rejection is respectfully requested.

On pages 6 and 7, the Office Action further details the rejection of Claims 14-23, 41, 47, 69, 95, 97, 98 and 99 and states that Applicants has disclosed a few cell lines that express Ad5 or Ad5/3 fiber, however, Applicant has not disclosed a sufficient number of different Ad species. The Office Action further states that Applicant has failed to disclose any specific inducible promoters.

Applicants disagree. For example, paragraph [0016] of the specification states that "it is also contemplated that the constructs and methods of the present invention will support the design and engineering of chimeric viral vectors which express amino acid residue sequences derived from two or more Ad serotypes." Paragraph [0021] of the specification states further that "in various embodiments, the adenovirus is a Group C adenovirus selected from serotypes 1, 2, 5 or 6; while in other embodiments, adenovirus selected from other serotypes, such as for example Ad37 (subgroup D) are useful as disclosed herein."

With respect to inducible promoters, many inducible promoters are known to those of skill in the art and thus need not be recited in the specification. Paragraph [0049] of the specification states that "stated another way, a nucleotide sequence of the present invention is one that encodes an expressible protein, polypeptide or fragment thereof, and it may further include an active constitutive or regulatable (e.g. inducible) promoter sequence."

The law is well settled that "[a] patent need not teach what is well known in the art". In a recent decision, the Federal Circuit clarified this rule in *Falker-Gunter Falkner v. Inglis* (Fed. Cir. 2006, 05–1324), wherein it held that that "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." The Court concluded that because "accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences, satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences."

Applicants respectfully submit that the specification meets Applicants' burden under 35 U.S.C. 112, first paragraph, and provides a sufficient number of species to support the presently pending claims.

On page 7, the Office Action further details the rejection of Claims 41, 47, 95, 98 and 99 and states that Applicant has not provided descriptive information for claimed tumor suppressor proteins, suicide proteins and biologically active fragments thereof.

Applicants respectfully disagree. The specification makes reference to tumor suppressor proteins or suicide proteins in at least the following locations: paragraphs 204, 205, 232, 237, 238 and 252.

As set forth above, The law is well settled that "[a] patent need not teach what is well known in the art". One of skill in the art would be aware that numerous literature sources are accessible which clearly provide, as of the filing date of the instant application, description for tumor suppressor proteins, suicide proteins and the nucleotide sequences which encode them. The law provides that the written description requirement does not require either the recitation or incorporation by reference of such genes and sequences.

Accordingly, Applicants respectfully submit that the specification meets Applicants' written description burden under 35 U.S.C. 112, first paragraph, and the rejection should therefore be withdrawn.

Claims 1, 4-8, 11, 14-23, 41, 47, 69, 95 and 97-101 stand rejected under U.S.C. §112, first paragraph as allegedly lacking enablement.

The first paragraph of 35 U.S.C. § 112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without undue experimentation (e.g., In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991). An invention is enabled even though the disclosure may require some routine experimentation to practice the invention. Hybritech Inc, V. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

In accordance with the accepted standards of enablement set forth above, an invention is enabled if one skilled in the art could make and use the claimed invention without undue experimentation. Applicants submit that one of skill in the art could make and use the subject matter of Claims 1, 4-8, 11, 14-23, 41, 47, 69, 95 and 97-101 without undue experimentation based on the information provided in the specification.

Claims 14-18, 20-23 and 69 stand rejected under U.S.C. §112, first paragraph as allegedly lacking enablement due to a lack of deposit of the packaging cell lines recited in the claims.

In accordance with the accepted standards of enablement set forth above, an invention is enabled if one skilled in the art could make and use the claimed invention without undue experimentation. Deposit of biological materials is not necessary if the materials, or starting materials, are known and readily available to the public, or obtainable by a repeatable method set forth in the specification. For the packaging cell lines recited in the claims, the complete nucleotide sequence of the plasmids used to modify the base cell line are recited in the specification. Plasmids pDV60, pDV67, pDV69, pDV80 and pDV90, were also deposited with ATCC as set forth in paragraph [0359] of the published application and provided in the Sequence Listing as follows: pDV60 (SEQ ID NO: 43), pDV67 (SEQ ID NO: 44), pDV69 (SEQ ID NO: 47), pDV80 (SEQ ID NO: 64) and pDV90 (SEQ ID NO: 65).

Applicants submit that one of skill in the art could make and use the subject matter of Claims 14-18, 20-23 and 69 without undue experimentation based on the specific information provided in the specification and claims and therefore the rejection should be withdrawn.

Claims 14-23, 41, 47, 69, 95, 97, 98 and 99 stand rejected under U.S.C. §112, first paragraph as allegedly lacking enablement for the reason set forth on page 11 of the Office Action, where it is stated that the specification enables the 293, 211, 211A, but not the A549, W163 Hela, Vero and other uncharacterized cell lines.

The specification teaches one of skill in the art how to make and use A549, W163 Hela, Vero and other uncharacterized cell lines, as set forth for example in paragraphs [0144] and [0294].

Compliance with the enablement requirement of Section 112, first paragraph, does not turn on whether an example is disclosed. (MPEP 2164.02). An applicant need not have actually reduced the invention to practice prior to filing. In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Applicants submit that one of skill in the art could make and use the subject matter of Claims 14-23, 41, 47, 69, 95, 97, 98 and 99 without undue experimentation based on the specific information provided in the specification and claims and therefore the rejection should be withdrawn.

Claims 1, 4-8, 11, 100 and 101 stand rejected under U.S.C. §112, first paragraph as allegedly lacking enablement for the reason set forth on page 12 and 13 of the Office Action, where it is stated that the specification, while being enabling for Ad5 TPL does not reasonably provide enablement for other TPL of different adenoviruses.

As set forth above, pCLF comprises an Ad2 leader sequence and an Ad5 fiber sequence. The corresponding cDNA sequence of the partial tripartite leader sequence found in pCLF is listed in SEQ ID NO: 8. (See paragraph 278 of the published version of the instant application; US Patent Pub. No. 20030157688). Hence the specification exemplifies to one of skill in the art how to make and use TPLs from Ad2 and Ad5. Examples of every possible TPL need not be required in order to meet the standard of enablement. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Rejection under 35 U.S.C. §103(a).

In the Office Action, the Examiner sets forth a number of grounds for rejection under 35 USC §103, each of which is discussed in detail as they apply to the current claims, below.

Claims 6-8 stand rejected under 35 USC § 103(a) as being obvious over Logan as evidenced by Clark for the reasons set forth on page 3 of the Office Action. The Office Action states that Calim 1 is nto limited to isolated nucleic acid molecules comprising an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides from different adenoviruses and thus Claims 6-8 would have been obvious for one of skill in the art relying on teh techaings of Logan as evidenced by Clark.

Applicants respectfully disagree. As stated in MPEP §2142, the examiner bears the initial burden of factually supporting a prima facie conclusion of obviousness. The examiner must show that the claimed invention was obvious to a person of ordinary skill in the art at the time the application was filed. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Neither Logan nor Logan as evidenced by Clark et al. discloses an isolated nucleic acid molecule wherein at least two different TPL exons are from different adenoviruses as required by Claim 1.

In a previous Office Action, the Examiner correctly indicated that Logan discloses plasmids pJAW43 and "sub 360-L1,2,3" which encodes a TPL leader sequence containing TPL exon 1 operatively linked to TPL exon 2 and 3, wherein the TPL exons 1 are from wild type adenovirus type 2. Furthermore, the Examiner correctly states that Logan fails to disclose a native adenovirus intron between the TPL exons but Clark et al. discusses a second native intron within the Ad2 TPL sequence and, thus, it is evident that two introns exist within the Ad2 TPL and that Logan et al., teach three exons (L1,2,3) within the Ad2 TPL.

Logan and Clark et al., disclose TPL exons and introns solely from adenovirus serotype 2. None of the vectors constructed and disclosed in Logan et al. contain TPL exons from more than one adenovirus serotype, as required by Claim 1, which Claims 6-8 depend from.

Thus, the Examiner has failed to set forth a prima facie case of obviousness and the rejection under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

Applicants submit that the application is now in condition for examination on the merits. Early notification of such action is earnestly solicited. If any issues remain which the Examiner feels may be best resolved through a personal or telephonic interview, the Examiner is respectfully requested to contact Applicants counsel, Linda R. Judge at (415) 836-2586.

Respectfully submitted,

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Dated: 7/5/06

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